



**INFORMATION DISCLOSURE STATEMENT**  
(Use several sheets if necessary)

Page 2

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624



**U.S. PATENT DOCUMENTS**

Examiner Initial*	Document Number	Date	Name	Class	Sub Class	Filing Date If Appropriate

**FOREIGN PATENT DOCUMENTS**

Document Number	Date	Country	Class	Sub Class	Translation Yes or No

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

<i>MB</i>	Nair N.P.V., Schwartz G., Dimitri R. et al. A dose-range finding study of zopiclone in insomniac patients. <i>Intl Clin Psychopharmacol</i> 1990; 5 (Suppl 2): 1-10.
<i>MB</i>	Martindale. The Extra Pharmacopoeia. The Royal Pharmaceutical Society, London 1996; 31 <sup>st</sup> edition: pp. 743-744.
<i>MB</i>	Houghton G.W., Dennis M.J., Templeton R., Martin B.K.. A repeated dose pharmacokinetic study of a new hypnotic agent, zopiclone (Imovane®). <i>Intl J Clin Pharmacol Therap Toxicol</i> 1985; 23: 97-100
<i>MB</i>	Marc-Aurèle J., Caille G., Bourgoïn J. Comparison of zopiclone pharmacokinetics in patients with impaired renal function and normal subjects. Effects of hemodialysis. <i>Sleep</i> 1987; 10 (Suppl 1): 22-26
<i>MB</i>	Parker G., Roberts C.J.C.. Plasmas concentrations and central nervous system effects of the new hypnotic agent zopiclone in patients with chronic liver disease. <i>Br J Clin Pharmacol</i> 1983; 16:259-265.
<i>MB</i>	Viron B., De Meyer M., Le Liboux A. et al., Steady-state pharmacokinetic of zopiclone during multiple oral dosing (7.5 mg nocte) in patients with severe chronic renal failure. <i>Intl Clin Pysychopharmacol</i> 1990; 5 (Suppl 2): 95-104.
<i>MB</i>	Sikdar S., Ruben S.M., Zopiclone abuse among polydrug users. <i>Addiction</i> 1996; 91: 285-286.

Examiner <i>Mark Ba</i>	Date Considered <i>7/6/01</i>
-------------------------	-------------------------------

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

RECEIVED

JUN 11 2001

TECH CENTER 1600/2900

**INFORMATION DISCLOSURE STATEMENT**  
(Use several sheets if necessary)

Page 3

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624



**U.S. PATENT DOCUMENTS**

Examiner Initial*	Document Number	Date	Name	Class	Sub Class	Filing Date If Appropriate

**FOREIGN PATENT DOCUMENTS**

Document Number	Date	Country	Class	Sub Class	Translation Yes or No

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

<i>MB</i>	Noble S., Langtry H.D., Lamb H.M., Zopiclone. An update of its pharmacology, clinical efficacy and tolerability in the treatment of insomnia. <i>Drugs</i> 198; 55:277-302.
<i>MB</i>	Fernandez C., Martin C., Gimenez F., Farinotti. Clinical pharmacokinetics of zopiclone, <i>Clin Pharmacokinet</i> 1995; 29: 431-441.
<i>MB</i>	Le Liboux Z., Frydman A., Gaillot J., Simultaneous Determination of Zopiclone and Its Two Major Metabolites (N-Oxide and N-Desmethyl) in Human Biological Fluids by Reversed-Phase High-Performance Liquid Chromatography, <i>J. Chromatography</i> , 417: (1987) 151-158.
<i>MB</i>	Musch B. and Maillard F., Zopiclone, The Third Generation Hypnotic: a Clinical Overview, <i>Intl. Clin. Psychopharmacol.</i> 5: 147-58 (1990)
<i>MB</i>	Julou L., Blanchard J.C., and Dreyfus J.F., Pharmacological and Clinical Studies of Cyclopyrrolones: Zopiclone and Suriclone, <i>Pharmacol., Biochem. &amp; Beh.</i> , 23: 653-659 (1985).
<i>MB</i>	Broadhurst A. and Cushnaghan R.C., Residual effects of Zopiclone (Imovane), <i>Sleep</i> , 10 (Suppl. 1): 48-53 (1987).
<i>MB</i>	Anderson A., Zopiclone and Nitrazepam: A Multicenter Placebo Controlled Comparative Study of Efficacy and Tolerance in Insomniac Patients in General Practice, <i>Sleep</i> , 10 (Suppl. 1): 54-62 (1987).
<i>MB</i>	Tamminen T. and Hensen P.P., Chronic Administration of Zopiclone and Nitrazepam in the Treatment of Insomnia, <i>Sleep</i> , 10 (Suppl. 1): 63-72 (1987).

Examiner

*Mark LBN*

Date Considered

*7/6/01*

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

RECEIVED

JUN 11 2001

TECH CENTER 1600/2900

# INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

Page 4

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624



## U.S. PATENT DOCUMENTS

Examiner Initial*	Document Number	Date	Name	Class	Sub Class	Filing Date If Appropriate
NB	5,786,357	7/28/98	Young et al.	514	249	12/1/92

## FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Sub Class	Translation Yes or No

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

NB	Inman W., Kubota K., Pearce G., Wilton W., PEM Report Number 10. Zopiclone, <i>Pharmacoevidemiol Drug Safety</i> 1993; 2: 499-521.
NB	Doble A., Canton T., Malgouris C., et al. The mechanism of action of zopiclone. <i>Eur Psychiat</i> 1995; 10 (Suppl 3): 117s-128s.
NB	Karle J. and Nielsen M., The Mechanism of Action and Pharmacology of Zopiclone, Rev. <i>Contemp. Pharmacother.</i> , Vol. 9, No. 2, pp. 77-87 (1998).
NB	Richards G., Schoch P., Haefely W., Benzodiazepine receptors: new vistas. <i>Sem Neurosci</i> 1991; 3: 191-203.
NB	Doble A., Martin I.L., <u>The GABA/benzodiazepine receptor as a target for psychoactive drugs.</u> RG Landes Company, Austin 1996; pp. 229-264.
NB	Langtry H.D., Benfield P., Zolpidem: A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential, <i>Drugs</i> , 1990; 40: 291-313.
NB	Blanchard J.C., Boireau A., Garret C., Julou L. <i>In vitro</i> and <i>in vivo</i> inhibition by zopiclone of benzodiazepine binding to rodent brain receptors. <i>Life Sci</i> 1979; 24: 2417-2420.
NB	Möhler H., Okada T. The benzodiazepine receptor in normal and pathological human brain. <i>Brit J Psychiat</i> 1978; 133: 261-268.
NB	Gaillot J., Le Roux Y., Houghton G.W., Dreyfus J.F.. Critical factors for pharmacokinetics of zopiclone in the elderly and in patients with liver and renal insufficiency. <i>Sleep</i> 1987; 10 (Suppl 1): 7-21.

Examiner	<i>Mark Ben</i>	Date Considered	7/6/01
*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

**INFORMATION DISCLOSURE STATEMENT**  
(Use several sheets if necessary)

Page 5

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624



**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date
MB	3,862,149	01/21/75	Cotrel et al.	260	2683Q	
MB	4,220,646	09/02/80	Cotrel et al.	424	250	
MB	5,786,357	07/28/98	Young et al.	514	219	

**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Country	Class	Sub Class	Trans. Yes	Trans. No
MB	EP 0 495 717	07/22/92	Europe				
MB	WO 93/10788	06/10/93	PCT				

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

MB	Doble et al., "The Pharmacology of Cyclopymrolone Derivatives Acting at the GABA <sub>A</sub> /Benzodiazepine Receptor," <i>Adv. Biochem. Psychopharmacol.</i> , 47:407-418 (1992).
MB	Gaillot et al., "Pharmacokinetics and Metabolism of Zopiclone," <i>Int. Pharmacophysiol.</i> 17:suppl. 2, pp. 76-91 (1982)/ <i>Pharmacology</i> 27:suppl. 2, pp. 76-91 (1983).
MB	E.J. Ariens, "Stereoselectivity in Pharmacodynamics and Pharmacokinetics," <i>Schweiz. Med. Wschr.</i> 120:131-134 (1990).
MB	Dragstedt, C.A. and Lang, V.F., "Respiratory Stimulants in Acute Cocaine Poisoning in Rabbits," <i>J. Pharmacol. Ex. Ther.</i> 32:215-222 (1928).
MB	Litchfield, J.T., Jr., and Wilcoxon, F., "A Simplified Method of Evaluating Dose-Effect Experiments," <i>J. Pharmacol. and Exp. Therap.</i> 96:99-113 (1949).
MB	Casarett and Doull's Toxicology: The Basic Science of Poisons, 5th ed. (1996) pp. 21-23.
MB	Prieur, David J. et al., "Procedures for Preclinical Toxicologic Evaluation of Cancer Chemotherapeutic Agents: Protocols of the Laboratory of Toxicology," <i>Cancer Chemotherapy Reports</i> , January 1973, part 3, vol. 4, no. 1:1-30.
MB	Everett et al., "Comparative Anticonvulsive Action of 3,5,5-Trimethyloxazolidine-2,4-Dione (Tridone), Dilantin and Phenobarbital," <i>J. Pharmacol.</i> 81:402 (1944).

Examiner	<i>Mark Ben</i>	Date Considered	<i>7/6/01</i>
<p>*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.</p>			

**INFORMATION DISCLOSURE STATEMENT**  
(Use several sheets if necessary)

Page 6

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624

**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date
MB	4,962,124	10/09/90	Sunshine et al.	514	568	
MB	5,102,890	04/07/92	Bourzat et al.	514	295	

**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Country	Class	Sub Class	Trans. Yes	Trans. No

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.):**

MB		Schwinn et al., "Functional Effects of Activation of Alpha-1 Adrenoceptors by Dexmedetomidine: In Vivo and In Vitro Studies," <i>J. Pharmacol. &amp; Exp. Therap.</i> , 259 (1991).
MB		Marley et al., "Differential Response to Flurazepam in Long-Sleep and Short-Sleep Mice," <i>Pharmacol. Biochem. &amp; Behav.</i> , 31:453-58 (1987).
MB		G. Zbinden et al., "Pharmacology of Benzodiazepines: Laboratory and Clinical Correlations," <i>Advances in Pharmacology</i> , 5:213-291 (1967).
MB		W.H. DeCamp, "The FDA Perspective on the Development of Stereoisomers," <i>Chirality</i> , 1:2-6 (1989).
MB		D.J. Birkett, "Racemates or Enantiomers: Regulatory Approaches," <i>Clinical and Experimental Pharmacology &amp; Physiology</i> , 16:479-483 (1989).
MB		R.F. Squires et al., "Benzodiazepine Receptors in Rat Brain," <i>Nature</i> , 266:732-734 (1977).
MB		R.E. Study et al., "Cellular Mechanisms of Benzodiazepine Action," <i>JAMA</i> , 247:2147-2151 (1982).
MB		D. Nutt, "Selective Ligands for Benzodiazepine Receptors: Recent Developments," <i>Curr. Aspects Neurosci.</i> , 2:259-293 (1990).

Examiner	<i>Mark Bess</i>	Date Considered	<i>7/6/01</i>
----------	------------------	-----------------	---------------

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.



**INFORMATION DISCLOSURE STATEMENT**  
(Use several sheets if necessary)

Page 7

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624

**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date
MB	5,331,000	07/19/94	Young et al.	514	570	

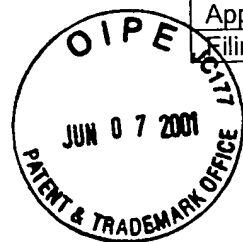
**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Country	Class	Sub Class	Trans. Yes	Trans. No

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

MB		G. Richards et al., "Role of GABA in the mechanism of benzodiazepine action," <i>Seminars in Neurosciences</i> , 3:191-203 (1991).
MB		J.T. Litchfield, "A Method for Rapid Graphic Solution of Time-Percent Effect Curves," <i>J. Pharmacol. and Exp. Therap.</i> , 97:399-408 (1949).
MB		G.W. Snedecor et al., <i>Statistical Methods</i> , 7th ed., 149.
MB		Fiche Technique No. 6, <i>J. Pharmacol. and Experim. Therap.</i> , 3:407-914 (1970).
MB		E.J. Ariens, "Racemic Therapeutics - ethical and regulatory aspects," <i>Eur. J. Clin. Pharmacol.</i> 41:89-93 (1991).
MB		C. Fernandez et al., "Determination of zopiclone enantiomers in plasma by liquid chromatography using a chiral cellulose carbonate column," <i>J. Chromatog.</i> , 572:195-202 (1991).
MB		P. Gauthier et al., "Influence of Zopiclone, a New Generation Hypnotic, on the Intermediate Stage and Paradoxical Sleep in the Rat," <i>Psychopharmacol.</i> , 130:139-143 (1997).
MB		Goodman & Gilman's, <i>The Pharmacological Basis of Therapeutics</i> , 8th ed. 346-349 (1990).
Examiner	M. L. B. B. B.	Date Considered 7/6/01

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.



**INFORMATION DISCLOSURE STATEMENT**  
(Use several sheets if necessary)

Page 8

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624



**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date

**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Country	Class	Sub Class	Trans. Yes	Trans. No

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

MB		C. Malgouris et al., "Autoradiographic Distribution of [3H]-Suridone Binding Sites in the Rat Brain," <i>Drug Develop. Res.</i> , 34:336-343 (1995).
MB		A. Doble et al., "The mechanism of action of zopiclone," <i>Eur. Psychiatry</i> , 10 Suppl. 3:117s-128s (1995).
MB		J.M. Stutzmann et al., "Pharmacological Properties and Mechanism of Action of the Cyclopyrrolones," <i>L. Encéphale</i> , XVIII:393-400 (1992).
MB		V. Bertolasi et al., "Stereochemistry of Benzodiazepine Receptor Ligands. Possible Role of C-H...X Interactions in Drug-Receptor Binding and Crystal Structures of CL 218-872, Zopiclone and DMCM," <i>J. Chem. Soc. Perkin Trans.</i> , 2:283-289 (1990).
MB		F. Jamali et al., "Enantioselective Aspects of Drug Action and Disposition: Therapeutic Pitfalls," <i>Journal of Pharmaceutical Sciences</i> , 78(9):695-715 (1989).
MB		A. Verma and S.H. Snyder, "Peripheral Type Benzodiazepine Receptors," <i>Annu. Rev. Pharmacol. Toxicol.</i> , 29:307-322 (1989).
MB		J.P. Brun, "Zopiclone, a Cyclopyrrolone Hypnotic: Review of Properties," <i>Pharmacology, Biochemistry and Behavior</i> , 29:831-832 (1988).
MB		P.A. Borea et al., "Stereochemical Features Controlling Binding and Intrinsic Activity Properties of Benzodiazepine-Receptor Ligands," <i>Molecular Pharmacology</i> , 31:334-344 (1987).

Examiner	<i>Mark Ubel</i>	Date Considered	<i>7/6/01</i>
*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.			



**INFORMATION DISCLOSURE STATEMENT**  
(Use several sheets if necessary)

Page 9

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624



**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date

**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Country	Class	Sub Class	Trans. Yes	Trans. No

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

MB		K.L. Goa and R.C. Heel, "Zopiclone, a Review of Its Pharmacodynamic and Pharmacokinetic Properties and Therapeutic Efficacy as an Hypnotic," <i>Drugs</i> , 32(1):48-65 (1986).				
MB		P. Jacqmin and M. Lesne, "Les Benzodiazepines: Aspects Pharmacodynamiques," <i>J. Pharm. Belg.</i> , 40(1):35-54 (1985).				
MB		L. Julou et al., "Pharmacological and Clinical Studies of Cyclopymolones: Zopiclone and Suriclone," <i>Pharmacology, Biochemistry and Behavior</i> , 23:653-659 (1985).				
MB		H. Kusnierczyk, "Antitumor Activity of Optical Isomers of Cyclophosphamide, Ifosfamide and Trofosfamide as Compared to Clinically Used Racemates," <i>J. Immunopharm.</i> , 8(4):455-480 (1986).				
MB		F. Jamali, "Pharmacokinetics of enantiomers of chiral non-steroidal anti-inflammatory drugs," <i>Eur. J. Drug Metab. and Pharmacokin</i> , 12(1):1-9 (1988).				
MB		D.W. Robertson et al., "Absolute Configurations and Pharmacological Activities of the Optical Isomers of Fluoxetine & Selective Serotonin-Uptake Inhibitor," <i>J. Med. Chem.</i> , 31:1412-1417 (1988).				
<table border="1"> <tr> <td>Examiner</td> <td><i>Mark Beal</i></td> <td>Date Considered</td> <td><i>7/6/01</i></td> </tr> </table>			Examiner	<i>Mark Beal</i>	Date Considered	<i>7/6/01</i>
Examiner	<i>Mark Beal</i>	Date Considered	<i>7/6/01</i>			
<p>*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.</p>						

**INFORMATION DISCLOSURE STATEMENT**  
(Use several sheets if necessary)

Page 10

TECH CENTER 160C/2900

JUN 11 2001

RECEIVED

Attorney No. Q62017	Serial No. 09/722,438
Applicant: Claude Cotrel, et al	
Filing Date: November 28, 2000	Group: 1624



**U.S. PATENT DOCUMENTS**

Examiner Initial*	Document Number	Date	Name	Class	Sub Class	Filing Date If Appropriate

**FOREIGN PATENT DOCUMENTS**

Document Number	Date	Country	Class	Sub Class	Translation Yes or No

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

MB	Braestrup C., Squires R.F.. Brain specific benzodiazepine receptors. <i>Brit J Psychiat</i> 1978; <b>133</b> : 249-260.
MB	Garzone P., Kroboth P., Pharmacokinetics of the Newer Benzodiazepines, <i>Clinical Pharmacokinetics</i> 16: 337-364 (1989).
MB	Miller L.G., Galpern W.R., Byrnes J.J., and Greenblatt, D.J., Benzodiazepine Receptor Binding of Benzodiazepine Hypnotics: Receptor and Ligand Specificity, <i>Pharmacology Biochem. And Beh.</i> Vol. 43, pp. 413-416, 1992.
MB	Greenblatt D.J., Divoll M., Abernethy D.R., Ochs H.R., and Shader R.I., Clinical Pharmacokinetics of the Newer Benzodiazepines, <i>Clin Pharmacokinetics</i> , 8: 233-252 (1983)
MB	Benavides, J., Peny B., Durand A. et al. Comparative <i>in vivo</i> and <i>in vitro</i> regional selectivity of central $\omega$ (benzodiazepine) site ligands in inhibiting [ <sup>3</sup> H]flumazenil binding in the rat central nervous system. <i>J Pharmacol Exp Therap</i> 1992; <b>263</b> : 884-896
MB	Ankier S.I., Goa K.L., Quazepam: A Preliminary Review of its Pharmacodynamic and Pharmacokinetic Properties, and Therapeutic Efficacy in Insomnia, <i>Drugs</i> 35: 42-62 (1988).
MB	Gaillot J., Heusse D., Houghton G.W. et al. Pharmacokinetics and metabolism of zopiclone. <i>Int Pharmacopsychiat</i> 1983; <b>17 (Suppl 2)</b> : 76-91.

Examiner	<i>Mark V. San</i>	Date Considered	<i>7/6/01</i>
----------	--------------------	-----------------	---------------

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.